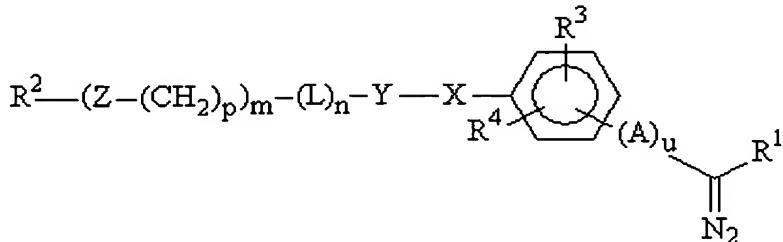


Amendments to the Claims:

The following listing of claims will replace all prior versions, and listings, of claims in the application:

1–25. (Canceled)

26. (Currently Amended) A temperature-stable labeling reagent of formula (0):



in which:

R^1 represents H or an alkyl, aryl or substituted aryl group,

R^2 represents a detectable label or at least two detectable labels interlinked by at least one multimeric structure, the detectable label being at least one label capable of directly or indirectly generating a detectable signal, and the detectable label being selected from the group consisting of an enzyme, a chromophore, a group with an electron density detectable by electron microscopy, a group with an electron density detectable by its electrical property, a radioactive molecule, and indirect systems,

L is a linker arm comprising a linear chain of at least two covalent bonds and n is an integer equal to 0 or 1,

R^3 and R^4 represent, independently of one another: H, NO₂, Cl, Br, F, I, R^2 - (L)_n-Y-X-, OR, SR, NR₂, R, NHCOR, CONHR, COOR, -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₃-CH₂-NH-R², or -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₄-CH₂-NH-R² with R = alkyl or aryl,

A is a linker arm comprising at least one covalent double bond enabling the conjugation of the diazo function with the aromatic ring and u is an integer between 0 and 2,

-Y-X- represents -CONH-, -NHCO-, -CH₂O-, or -CH₂S-,

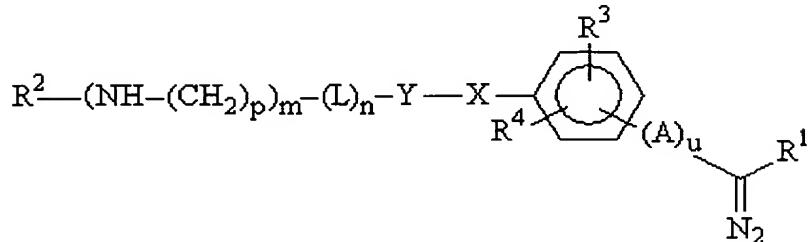
-Z- represents -NH-, -NHCO-, or -CONH-,

m is an integer between ~~1 and 10~~ 2 and 10, and

p is an integer between 1 and 10.

27. (Currently Amended) The labeling reagent according to claim 26, of formula

(1):



in which:

R¹ represents H or an alkyl, aryl or substituted aryl group,

R² represents a detectable label or at least two detectable labels interlinked by at least one multimeric structure,

L is a linker arm comprising a linear chain of at least two covalent bonds and n is an integer equal to 0 or 1,

R³ and R⁴ represent, independently of one another: H, NO₂, Cl, Br, F, I, R² - (L)_n-Y-X-, OR, SR, NR₂, R, NHCOR, CONHR, COOR, -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₃-CH₂-NH-R², or -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₄-CH₂-NH-R² with R = alkyl or aryl, and

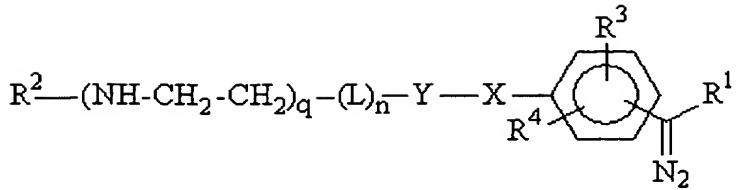
-Y-X- represents -CONH-, -NHCO-, -CH₂O-, or -CH₂S-,

m is an integer between ~~1 and 10~~ 2 and 10, and

p is an integer between 1 and 10.

28. (Previously Presented) The reagent according to claim 27, wherein p is less than or equal to m.

29. (Currently Amended) The reagent according to claim 27, of formula (2):



in which:

R^1 represents H or an alkyl, aryl or substituted aryl group,

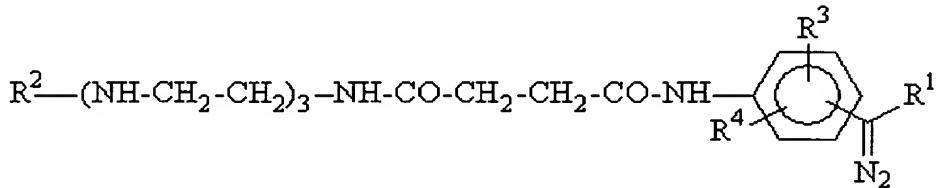
R^2 represents a detectable label or at least two detectable labels interlinked by means of at least one multimeric structure,

L is a linker arm comprising a linear chain of at least two covalent bonds and n is an integer equal to 0 or 1,

R^3 and R^4 represent, independently of one another: H, NO₂, Cl, Br, F, I, R² - (L)_n-Y-X-, OR, SR, NR₂, R, NHCOR, CONHR, COOR, -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₃-CH₂-NH-R², or -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₄-CH₂-NH-R² with R = alkyl or aryl, and

q is an integer between 2 and 10 and 1 and 10.

30. (Previously Presented) The reagent, according to claim 29, of formula (3):



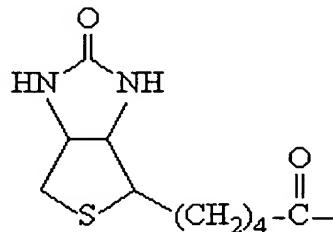
in which:

R^1 represents H or an alkyl, aryl or substituted aryl group,

R^2 represents a detectable label or at least two detectable labels interlinked by means of at least one multimeric structure,

R^3 and R^4 represent, independently of one another: H, NO₂, Cl, Br, F, I, R² - (L)_n-Y-X-, OR, SR, NR₂, R, NHCOR, CONHR, COOR, -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₃-CH₂-NH-R², or -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₄-CH₂-NH-R² with R = alkyl or aryl.

31. (Previously Presented) The reagent according to claim 30, wherein R² consists of a D-biotin residue of formula (4):



32. (Previously Presented) The reagent according to claim 31, wherein R¹ is CH₃, and R³ and R⁴ each represent H.

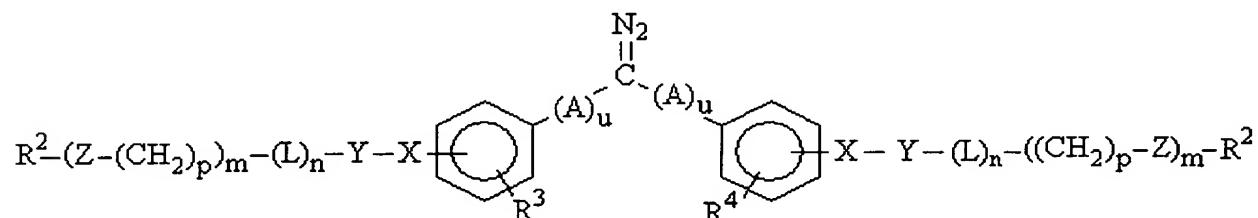
33. (Withdrawn) The reagent according to claim 29, in which the structure -(L)_n- consists of:

spermine or N,N'-bis(3-aminopropyl)-1,4-diaminobutane: NH₂-(CH₂)₃-NH-(CH₂)₄-NH-(CH₂)₃-NH₂, or

spermidine or N-(3-aminopropyl)-1,4-butanediamine: H₂N-(CH₂)₄-NH-(CH₂)₃-NH₂, or

a derivative containing an alanine motif: NH₂-CH₂-CH₂-COOH.

34. (Withdrawn-Currently Amended) A temperature-stable labeling reagent of formula (6):



in which:

R² represents a detectable label or at least two detectable labels interlinked by at least one multimeric structure, the detectable label being at least one label capable of

directly or indirectly generating a detectable signal, and the detectable label being selected from the group consisting of an enzyme, a chromophore, a group with an electron density detectable by electron microscopy, a group with an electron density detectable by its electrical property, a radioactive molecule, and indirect systems,

L is a linker arm comprising a linear chain of at least two covalent bonds and n is an integer equal to 0 or 1,

R^3 and R^4 represent independently of one another: H, NO₂, Cl, Br, F, I, R² - (L)_n-Y-X-, OR, SR, NR₂, R, NHCOR, CONHR, COOR, -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₃-CH₂-NH-R², or -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₄-CH₂-NH-R² with R = alkyl or aryl,

A is a linker arm comprising at least one covalent double bond enabling the conjugation of the diazo function with the aromatic ring and u is an integer between 0 and 2,

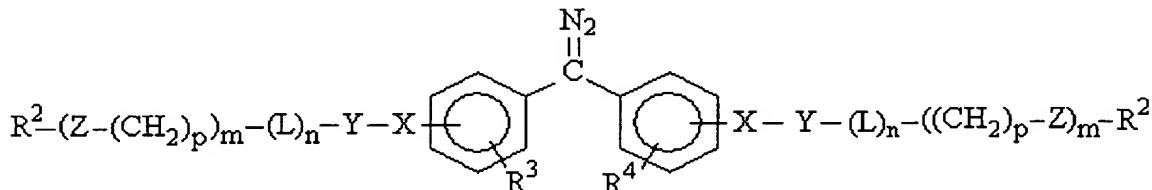
-Y-X- represents -CONH-, -NHCO-, -CH₂O-, or -CH₂S-,

-Z- represents -NH-, -NHCO-, or -CONH-,

m is an integer between 2 and 10 and 10, and

p is an integer between 1 and 10.

35. (Withdrawn-Currently Amended) The labeling reagent, according to claim 34, of formula (7):



in which:

R^2 represents a detectable label or at least two detectable labels interlinked by at least one multimeric structure,

L is a linker arm comprising a linear chain of at least two covalent bonds and n is an integer equal to 0 or 1,

R³ and R⁴ represent, independently of one another: H, NO₂, Cl, Br, F, I, R² - (L)_n-Y-X-, OR, SR, NR₂, R, NHCOR, CONHR, COOR, -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₃-CH₂-NH-R², or -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₄-CH₂-NH-R² with R = alkyl or aryl,

-Y-X- represents -CONH-, -NHCO-, -CH₂O-, or -CH₂S-,

-Z- represents -NH-, -NHCO-, or -CONH-,

m is an integer between 2 and 10~~1 and 10~~, and

p is an integer between 1 and 10.

36. (Withdrawn) The reagent according to claim 26, wherein:

L comprises a motif -(O-CH₂-CH₂)-, repeated from 1 to 20 times, and

-Z- is -NH-, -NHCO- or -CONH-.

37. (Withdrawn) The reagent according to claim 34, wherein:

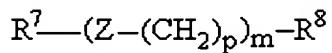
L comprises a motif -(O-CH₂-CH₂)-, repeated from 1 to 20 times, and

-Z- is -NH-, -NHCO- or -CONH-.

38. (Withdrawn-Currently Amended) A method for the synthesis of a labeling reagent according to claim 26, comprising the following steps:

a) providing a label or a label precursor having a reactive function R⁶,

b) providing a linker arm of formula (8):



in which:

-Z- represents -NH-, -NHCO-, or -CONH-,

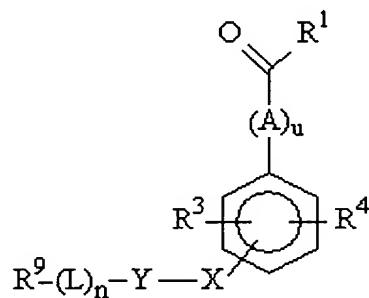
m is an integer between 2 and 10~~1 and 10~~,

p is an integer between 1 and 10,

R^7 and R^8 represent two reactive functions which may be identical or different,

c) reacting together the reactive function R^6 of said label or label precursor and the function R^7 of the linker arm of formula (8) in the presence of at least one coupling agent to form a covalent bond, R^6 and R^7 being complementary,

d) providing a derivative of formula (9):



in which:

R^1 represents H or an alkyl, aryl or substituted aryl group,

L is a linker arm comprising a linear chain of at least two covalent bonds and n is an integer equal to 0 or 1,

R^3 and R^4 represent, independently of one another: H, NO₂, Cl, Br, F, I, R²-(L)_n-Y-X-, OR, SR, NR₂, R, NHCOR, CONHR, COOR, -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₃-CH₂-NH-R², or -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₄-CH₂-NH-R² with R = alkyl or aryl,

-Y-X- represents -CONH-, -NHCO-, -CH₂O-, or -CH₂S-,

A is a linker arm comprising at least one covalent double bond enabling the conjugation of the diazomethyl function with the aromatic ring and u is an integer equal to 0 or 1, and

R^9 represents a reactive function complementary to R^8 ,

e) reacting together the reactive function R⁹ of the derivative of formula (9) and the function R⁸ of the linker arm of formula (8) in the presence of at least one coupling agent to form a covalent bond,

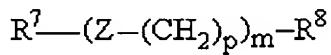
f) reacting the hydrazine or one of its derivatives with the ketone or aldehyde function to form a hydrazone, and

g) converting the hydrazone to a diazomethyl function by means of an appropriate treatment.

39. (Withdrawn-Currently Amended) A method for the synthesis of a labeling reagent according to claim 34, comprising the following steps:

a) providing a label or a label precursor having a reactive function R⁶,

b) providing a linker arm of formula (8):



in which:

-Z- represents -NH-, -NHCO-, or -CONH-,

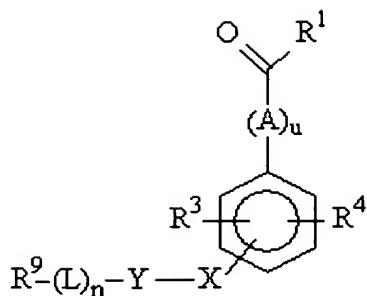
m is an integer between 2 and 10 ~~1 and 10~~,

p is an integer between 1 and 10,

R⁷ and R⁸ represent two reactive functions which may be identical or different,

c) reacting together the reactive function R⁶ of said label or label precursor and the function R⁷ of the linker arm of formula (8) in the presence of at least one coupling agent to form a covalent bond, R⁶ and R⁷ being complementary,

d) providing a derivative of formula (9):



in which:

R^1 represents H or an alkyl, aryl or substituted aryl group,

L is a linker arm comprising a linear chain of at least two covalent bonds and n is an integer equal to 0 or 1,

R^3 and R^4 represent, independently of one another: H, NO_2 , Cl, Br, F, I, $\text{R}^2-(\text{L})_n-\text{Y}-\text{X}-$, OR, SR, NR_2 , R, NHCOR , CONHR , COOR , $-\text{CO-NH-(CH}_2)_3-(\text{O-CH}_2\text{-CH}_2)_3\text{-CH}_2\text{-NH-R}^2$, or $-\text{CO-NH-(CH}_2)_3-(\text{O-CH}_2\text{-CH}_2)_4\text{-CH}_2\text{-NH-R}^2$ with $\text{R} =$ alkyl or aryl,

$-\text{Y-X-}$ represents $-\text{CONH-}$, $-\text{NHCO-}$, $-\text{CH}_2\text{O-}$, or $-\text{CH}_2\text{S-}$,

A is a linker arm comprising at least one covalent double bond enabling the conjugation of the diazomethyl function with the aromatic ring and u is an integer equal to 0 or 1, and

R^9 represents a reactive function complementary to R^8 ,

e) reacting together the reactive function R^9 of the derivative of formula (9) and the function R^8 of the linker arm of formula (8) in the presence of at least one coupling agent to form a covalent bond,

f) reacting the hydrazine or one of its derivatives with the ketone or aldehyde function to form a hydrazone, and

g) converting the hydrazone to a diazomethyl function by means of an appropriate treatment.

40. (Withdrawn) The method of synthesis according to claim 38, further comprising:
an additional step consisting of protection of the ketone or aldehyde function of compound (9), and
a subsequent additional step consisting of deprotection of said ketone or aldehyde function.

41. (Withdrawn) The method of synthesis according to claim 39, further comprising:
an additional step consisting of protection of the ketone or aldehyde function of compound (9), and
a subsequent additional step consisting of deprotection of said ketone or aldehyde function.

42. (Withdrawn) A method for the labeling of a biological molecule, comprising bringing into contact, in a homogeneous solution in a substantially aqueous buffer, the biological molecule and a reagent according to claim 26.

43. (Withdrawn) A method for the labeling of a biological molecule, comprising bringing into contact, in homogeneous solution in a substantially aqueous buffer, a biological molecule and a reagent according to claim 34.

44. (Withdrawn) A labeled biological molecule which can be obtained by the method according to claim 42.

45. (Withdrawn) A labeled biological molecule which can be obtained by the method according to claim 43.

46. (Withdrawn) A method for the labeling and fragmentation of a single-stranded or double-stranded nucleic acid, the method comprising:
fragmenting the nucleic acid,

attaching a label to at least one of the fragments by means of a labeling reagent chosen from the reagents according to claim 26,

said reagent coupling covalently and predominantly on at least one phosphate of said fragment.

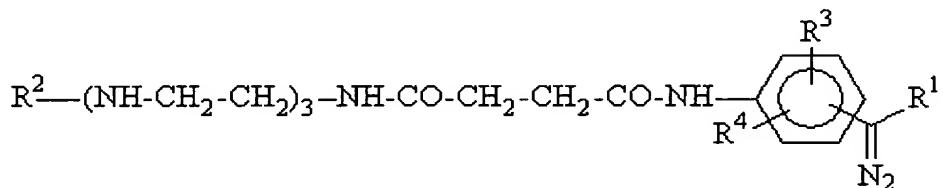
47. (Withdrawn) A method for the labeling and fragmentation of a single-stranded or double-stranded nucleic acid, the method comprising:

fragmenting the nucleic acid,

attaching a label to at least one of the fragments by means of a labeling reagent chosen from the reagents according to claim 34,

said reagent coupling covalently and predominantly on at least one phosphate of said fragment.

48. (Withdrawn) The method according to claim 46, wherein the labeling reagent is chosen from the compounds of formula (3):



in which:

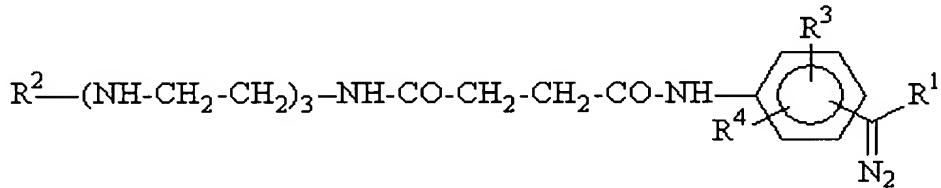
R^1 represents H or an alkyl, aryl or substituted aryl group,

R^2 represents a detectable label or at least two detectable labels interlinked by at least one multimeric structure,

L is a linker arm comprising a linear chain of at least two covalent bonds and n is an integer equal to 0 or 1, and

R^3 and R^4 represent, independently of one another: H, NO₂, Cl, Br, F, I, R² - (L)_n-Y-X-, OR, SR, NR₂, R, NHCOR, CONHR, COOR, -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₃-CH₂-NH-R², or -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₄-CH₂-NH-R² with R = alkyl or aryl.

49. (Withdrawn) The method according to claim 47, wherein the labeling reagent is chosen from the compounds of formula (3):



in which:

R^1 represents H or an alkyl, aryl or substituted aryl group,

R^2 represents a detectable label or at least two detectable labels interlinked by at least one multimeric structure,

L is a linker arm comprising a linear chain of at least two covalent bonds and n is an integer equal to 0 or 1, and

R^3 and R^4 represent, independently of one another: H, NO₂, Cl, Br, F, I, R² - (L)_n-Y-X-, OR, SR, NR₂, R, NHCOR, CONHR, COOR, -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₃-CH₂-NH-R², or -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₄-CH₂-NH-R² with R = alkyl or aryl.

50. (Withdrawn) The method according to claim 48, wherein the fragmentation and the labeling are carried out in two steps.

51. (Withdrawn) The method according to claim 49, wherein the fragmentation and the labeling are carried out in two steps.

52. (Withdrawn) The method according to claim 48, wherein the fragmentation and the labeling are carried out in one step.

53. (Withdrawn) The method according to claim 49, wherein the fragmentation and the labeling are carried out in one step.

54. (Withdrawn) The method according to claim 50, wherein the labeling is carried out in a substantially aqueous homogeneous solution.

55. (Withdrawn) The method according to claim 52, wherein the labeling is carried out in a substantially aqueous homogeneous solution.

56. (Withdrawn) The method according to claim 51, wherein the labeling is carried out in a substantially aqueous homogeneous solution.

57. (Withdrawn) The method according to claim 50, wherein the fragmentation is carried out by an enzymatic, physical, or chemical process.

58. (Withdrawn) The method according to claim 51, wherein the fragmentation is carried out by an enzymatic, physical, or chemical process.

59. (Withdrawn) A labeled nucleic acid obtained by the method according to claim 46.

60. (Withdrawn) A labeled nucleic acid obtained by the method according to claim 47.

61. (Withdrawn) A kit for the detection of a target nucleic acid, comprising a labeled nucleic acid according to claim 59.

62. (Withdrawn) A kit for the detection of a target nucleic acid, comprising a labeled nucleic acid according to claim 60.

63. (Withdrawn) A solid support to which is attached a reagent according to claim 26.

64. (Withdrawn) A solid support to which is attached a reagent according to claim 34.

65. (Withdrawn) A method for the capture of nucleic acids, comprising:

providing a solid support to which is directly or indirectly attached at least one biological molecule according to claim 44, the biological molecule or the nucleic acid comprising a diazomethyl function,

bringing into contact a biological sample which may contain free nucleic acids,
and

washing the solid support where the molecule(s) is (are) covalently attached at least to a nucleic acid.

66. (Withdrawn) A method for the capture of nucleic acids, comprising the following steps:

providing a solid support to which is directly or indirectly attached at least one biological molecule according to claim 45, the biological molecule or the nucleic acid comprising a diazomethyl function,

bringing into contact a biological sample which may contain free nucleic acids,
and

washing the solid support where the molecule(s) is (are) covalently attached at least to a nucleic acid.